UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/545,199	04/06/2000	David E. Lowery	28341/6227.1NCP	9014

7590 06/13/2003

Joseph A Williams Jr
Marshall O'Toole Gerstein Murray and Borun
6300 Sears Tower
233 South Wacker Drive
Chicago, IL 60606-6402

EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	23

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/545,199	Applicant(s) Lowery et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 31, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *7-24 and 31-33* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *7-24 and 31-33* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-6, 25-30 and 34-51 have been canceled.

Claims 7-12, 14-18, 20-24 and 31 have been amended.

Claims 7-24 and 31-33 are pending and under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 31, 2003 has been entered.

Objections and Rejections Withdrawn

3. Claims 31-33 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for depending from a canceled has been obviated through amendment of claim 31 to depend from any one of claims 7-24.

4. Claims 1,3-6 rejected under 35 U.S.C. 112, first paragraph (scope, vaccine), because the specification, while being enabling for the introduction of mutations into specific open reading frames, specifically the elected SEQ ID NO3, for the production of an immunogenic recombinant bacteria, does not reasonably provide enablement for formulation of vaccines for any gram negative bacteria, with any mutation in SEQ ID NO 3 or a species homolog of SEQ ID No 3 for the induction of a protective immune response, the full genus of which has not been enabled as vaccine compositions, in light of the claims having been canceled.

5. Claims 1, 3-6 rejected under 35 U.S.C. 112, first paragraph (written description, scope), as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention,in light of the claims having been canceled.

6. Claims 1, 3-6 rejected under 35 U.S.C. 112, second paragraph reciting the phrase "a gene", that evidences decreased expression, in light of the claims still reciting the term homolog and expression of the homolog gene product which has not been defined;in light of the claims having been canceled.

7. Claims 1, 3-6 rejected under 35 U.S.C. 112, second paragraph in light of the mutation in the homolog gene and gene product, which results in decreased expression, are not clearly set forth in the claims, in light of the claims having been canceled.

8. Claims 8, 14, 20 rejected under 35 U.S.C. 112, second paragraph depend from claim 7, and define the mutation to result in "decreased activity of the gene product", in light of the amendment of claims 7, 8, 14 and 20 to define the decreased activity to be due to decreased expression.

9. Claims 1, 3-5, 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamoto et al (1993), in light of claims 1, 3-5 having been canceled, and claims 31-32 having been amended to depend from claim 7.

Rejections Maintained

10. Claims 32-33 rejected under 35 U.S.C. 112, first paragraph (scope, vaccine), because the specification, while being enabling for the introduction of mutations into specific open reading frames, specifically the elected SEQ ID NO3, for the production of an immunogenic recombinant bacteria, does not reasonably provide enablement for formulation of vaccines for any gram negative bacteria, with any mutation in SEQ ID NO 3 or a species homolog of SEQ ID No 3 for the induction of a protective immune response, the full genus of which has not been enabled as vaccine compositions, for reasons of record in paper number 15, paragraph 8.

7-24, 31-33

11. Claims ~~7-33~~ rejected under 35 U.S.C. 112, first paragraph (written description, scope), as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record in paper number 15, paragraph 9.

12. Claims 8-24, 31-33 rejected under 35 U.S.C. 112, second paragraph reciting the phrase "a gene" that evidences decreased expression, in light of the claims still reciting the term homolog and expression and activity of the homolog gene product which has not been defined; for reasons of record in paper number 15, paragraph 10, page 11, second paragraph.

13. Claims 8-24, 31-33 rejected under 35 U.S.C. 112, second paragraph in light of the mutation in the homolog gene and gene product, which results in decreased expression, are not clearly set forth in the claims, see paper number 15, paragraph 10.

Response to Arguments

14. Applicant's arguments filed March 31, 2003 have been fully considered but they are not persuasive.

15. The rejection of claims 31-33 under 35 U.S.C. 112, first paragraph (scope, vaccine directed to homolog mutations, any gram negative bacterium with a atpG mutation, or homolog mutation), because the specification, while being enabling for the introduction of mutations into specific open reading frames, specifically the elected SEQ ID NO3, for the production of an immunogenic recombinant bacteria, does not reasonably provide enablement for formulation of vaccines for any gram negative bacteria, with any mutation in SEQ ID NO 3 or a species homolog of SEQ ID No 3 for the induction of a protective immune response, the full genus of which has not been enabled as vaccine compositions, is

traversed on the grounds that "paragraph 4 of the Office Action, claims 7-24 and 31-33 are enabled by the specification."

16. It is the position of the examiner that the withdrawal of a portion of the scope of enablement was removed over claims 31-33 based upon the amendment of the claims to recite limitations directed to an attenuated Pasteurellaceae bacteria with a mutation in the atpG coding sequence, but a different scope of enablement over claims 31-33 was maintained in paragraph 15 of the same Office Action based on the fact that the instant specification has not enabled the formulation of the claimed genus compositions into vaccines, for reasons of record in paper number 19, paragraph 15 and 22-23; and paper number 15, paragraph 8.

17. The rejection of claims 7-33 under 35 U.S.C. 112, first paragraph (written description, scope), as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is traversed on the grounds that "the written description analysis that is specifically applicable for nucleic acids and that this analysis is not appropriate for all "genus" subject matter. The claimed invention relates to attenuated gram negative bacteria and vaccine compositions comprising the bacteria and not to polynucleotides per se." and concludes that there is no

need to precisely define the chemical structure of every atpG gene in every bacteria or vaccine.

18. It is the position of the examiner that the patentable novelty of the instant Application is directed to mutations in a polynucleotide sequence that encodes for the gamma subunit of ATPase of Pasteurella moltocida, that is taught to have a possible, potential, gene function of atpG (see Table 1, page 37, instant specification, bottom of page) and SEQ ID No 132, obtained from Actinobacillus pleuropneumonia.

The claimed invention is directed mutations that effect gene products. Clearly the instantly claimed invention is directed to subject matter that is specifically applicable for nucleic acids. The written description analysis set forth in the First Office action is clearly applicable to the claimed invention that is directed to atpG genes in gram negative bacteria not described or known in the art, as well as homolog products not defined to have any specific homologous function or sequence.

With respect to defining a representative number of species to describe the now claimed genus of mutated gram negative bacteria, it is the position of the examiner that no specific genes (open reading frames) that encode species homologs of the identified nucleic acid sequences meet the written description requirement by providing a representative number of species of the claimed genus recombinant bacteria with mutations in species homologs of nucleic acid sequences of SEQ Id No 3 and are mutated to evidence reduced gene product activity, and/or reduced expression of the encoded gene product. Adequate written description requires

more than a mere statement that it is part of the invention and a reference to a potential method of isolating the nucleic acid molecule. The nucleic acid that encodes the gene product itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. The rejection is maintained for reasons of record. Amendment of the claims directed to material that has been described in the instant specification could obviate this rejection and removal of the phrase "or a species homolog thereof".

Additionally Pasteurellaceae is a term that represents a FAMILY of bacteria which comprises 100s of species of bacteria of various genera. The claims recite "a species homolg thereof"; the recitation of a FAMILY of bacteria does not define what the species homolog coding sequences are, for each of the Pasteurellaceae members claimed. Each genome is organized and contains coding sequences that differ one from the other based on differences both at the genera and species level. Where and how the mutations can be introduced into the chromosomal DNA, of the recited species homolog coding sequences have not been described. The person of skill in the art would have to de novo identify and determine how and where an atpG coding sequence homolog is located in the recited FAMILY of bacteria before the mutation could or would be introduced.

The lack of written description rejection is maintained for reasons of record.

19. The rejection of claims 8-24, 31-33 under 35 U.S.C. 112, second paragraph for reciting the phrase "a gene", is asserted to have been obviated through amendment of the claims to recite "a mutation in the atpG protein coding region of SEQ ID No 3" , and claim 7, further having been amended to recite "resulting in decreased atpG biological activity".

20. It is the position of the examiner that this rejection was partially obviated through amendment of the claims to recite the phrase "a mutation in the atpG protein coding region of SEQ ID No 3", but the claims still recite the phrase "or species homologs thereof". While it is clear that within the scope of the claims there is now a defined gene product of atpG, what the "species homolog" is and what the species homolog "gene product" is, is still unclear.

A species homolog of atpG could be atpA, B, C, D, E, or F which share a conserved sequence. A mutation in the channel forming subunits of atp would result in a decrease atpG activity (transport of hydrogen), as the channel forming proteins being dysfunctional disallowing the atpG encoded protein from functioning. Though the amendment partially obviated the rejection, that portion of the rejection that has not been obviated is maintained for reasons of record.

21. The rejection of claims 7-24, 31-33 rejected under 35 U.S.C. 112, second paragraph, for the recitation of the phrase "decreased activity of a gene product"(claims 7, 9-24 and 31-33, and questioned what gene product must be expressed (claims 31-33 have been

amended to recite "decreased expression) is traversed on the grounds that the claims have been amended to recite that the mutation is in the atpG coding sequence, and to "evidence decreased activity or decreased expression" which clarifies what the gene product and what must be expressed.

22. It is the position of the examiner that through amendment of the claims to recite the phrase "a mutation in the atpG protein coding region", the rejection under 112, second paragraph was partially obviated. While the combination of claims 7 and 8 now define the gene product to evidence decreased activity due to decreased expression, this combination of claim limitation is still unclear because where the mutation that will decrease gene product expression is not distinctly claimed; a second mutation could be in the promoter region of the gene/operon in which the atpG coding sequence is located and what has been mutated in claim 1 is the coding sequence. It appears that the bacteria of claim 8 has two mutations, or a mutation outside the coding sequence of atpG. Additionally, where in the species homolog(s) the mutation(s) is/are located has not been clearly set forth in the claims.

23. The rejection of claims 8, 14, 20 under 35 U.S.C. 112, second paragraph, for reciting that a single mutation would result in "decreased activity of the gene product" and result in "decreased expression of a gene" is traversed on the grounds that "the dependent claims are further limitations of the decrease in activity, not additional mutations", that "a

decrease in expression of a gene product does reduce the overall activity of the gene product in some manner, be it inherent enzymatic activity or subsequent downstream activity" and "a decrease in gene expression could result from a mutation which almost completely abolishes gene expression, thereby resulting in no gene product being produced and thus no activity".

24. It is the position of the examiner that through the recitation of "decreased activity (claim 7)" the claims include within the scope, gene expression of a product with activity and gene expression product without activity. The dependent claims which recite that the mutation effects expression of the gene product, resulting in decreased expression, need not be limited to decreased expression equals decreased activity, but includes within the scope an additional mutation of the promoter so that the amount of expressed product is reduced. While Applicant's arguments are clear, the claimed invention is not. An amendment of the claim to recite a phrase that sets forth the concept

--wherein the activity is decreased due to decreased gene expression-- rather than setting forth claim limitations that redefine the mutation to be one that effects expression rather than activity could obviate this rejection. A bacterium with a plurality of mutations, clearly supported by the specification could be claimed as having more than one mutation. While expression can influence product activity, the claim language recited does not show a clear delineation as to what type of mutation is being introduced into the claimed bacterium.

New Claim Limitations/New Grounds of Rejection

Claim Rejections - 35 U.S.C. § 112

25. Claims 8-12 14-18 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-12 depend from claim 7 and recite the phrase "decreased gene expression of an atpG gene product"; the word gene lacks antecedent basis in claim 7 from which they depend. Claims 14-18 depend from claims 13 and 7, and recite the phrase "atpG gene"; this phrase lacks antecedent basis in claims 7 and 13 from which claims 14-18 depend. The phrase was deleted by amendment. Claims 21-24 depend from claims 19, 13, and 7 and recite the phrase "atpG gene"; this phrase lacks antecedent basis in claims 7, 13 and 19 from which claims 21-24 depend. The phrase was deleted by amendment.

Claim 8 broadens the scope of claim 7 from which depends by defining the mutation to be "decreased gene expression". The phrase encompasses a mutation in the promoter region of the gene operon, and not in the protein coding region as defined in independent claim 7. Claim 8 should recite the phrase --further comprising an additional mutation which reduces expression through an additional mutation in SEQ ID NO 3-- or an equivalent phrase. What mutation causes the decreased gene expression? What is the mutation in the species homolog that results in reduced gene expression?

Conclusion

26. This is non-final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
June 11, 2003

LZS
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600